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Comparative study on Carbetocin vs oxytocin in prevention of postpartum haemorrhage

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ABSTRACT

Background: Postpartum hemorrhage (PPH) is a leading cause of maternal mortality globally, particularly in low-resource settings where effective, stable uterotonic agents are essential.**Objective:** This study compares the efficacy and safety of carbetocin and oxytocin in preventing PPH among patients at Durgapur Steel Plant Hospital, Durgapur, West Bengal.**Method:** A randomized controlled trial was conducted from January 2023 to December 2023 with 100 patients, divided equally into two groups: carbetocin (50) and oxytocin (50). Both drugs were administered intramuscularly post-delivery, and blood loss was measured over the first 24 hours.**Results:** Patients in the carbetocin group showed a significantly lower average blood loss (290 mL) compared to the oxytocin group (340 mL), with a relative reduction of 14.7% ($p<0.05$). Only 12% of the carbetocin group required additional uterotonics, in contrast to 24% in the oxytocin group. Side effects were slightly less frequent with carbetocin, observed in 8% of patients, versus 10% in the oxytocin group. Overall, carbetocin demonstrated enhanced stability and efficacy, with a lower incidence of PPH-related complications (10%) compared to oxytocin (18%).**Conclusions:** Carbetocin proved more effective than oxytocin in reducing blood loss and the need for additional uterotonics in PPH prevention, suggesting its potential as a preferable choice in clinical settings.

Keywords: Postpartum hemorrhage, carbetocin, oxytocin, maternal health, uterotonic agents

INTRODUCTION

Postpartum hemorrhage (PPH) is one of the most significant threats to maternal health globally, accounting for roughly a quarter of maternal deaths, with the highest incidences observed in low- and middle-income countries [1]. Defined by the loss of more than 500 mL of blood within 24 hours of vaginal birth or over 1000 mL post-cesarean, PPH can quickly escalate into a life-threatening situation if not promptly managed. The importance of effective PPH prevention is underscored by its place in the United Nations Sustainable Development Goals, which target a reduction in maternal mortality to less than 70 per 100,000 live births by 2030, emphasizing a pressing need for scalable and effective interventions [2]. Prevention of PPH, therefore, has been at the forefront of obstetric research and healthcare policy, particularly focusing on finding uterotonic agents that are both effective and accessible across various healthcare environments.

Oxytocin, a naturally occurring hormone, has long been the gold standard for uterotonic therapy due to its efficacy, widespread availability, and relatively low cost. When administered immediately postpartum, oxytocin induces contractions in the uterine smooth muscle, helping to reduce blood loss by promoting uterine involution. Typically given via intravenous or intramuscular injection, oxytocin's rapid onset of action has proven effective in emergency obstetric care [3]. However, the drug's short half-life necessitates either continuous infusion or repeated doses to maintain its effectiveness in sustaining uterine contraction, especially in high-risk cases [4]. Additionally, oxytocin is sensitive to temperature and requires cold storage to preserve its potency, a condition that poses significant logistical challenges in settings where refrigeration is not reliably available, such as rural healthcare facilities in low-resource countries.

To address some of the limitations associated with oxytocin, carbetocin, a synthetic analog of oxytocin, has been developed as an alternative uterotonic agent. Carbetocin's mechanism of action closely resembles that of oxytocin, as it binds to oxytocin receptors in the uterine muscle to stimulate contractions. However, carbetocin boasts a longer half-life, allowing for sustained uterine contraction with a single dose, thereby reducing the need for repeated administrations or continuous infusions [5]. This extended duration is particularly advantageous in settings with limited access to continuous monitoring or infusion equipment [6]. Moreover, carbetocin is stable at room temperature, offering a significant benefit in regions where cold-chain infrastructure is either lacking or unreliable. In a large-scale randomized controlled trial conducted by the Vogel in, heat-stable carbetocin demonstrated efficacy comparable to oxytocin in preventing PPH, with the added benefit of maintaining stability without refrigeration.

The stability of carbetocin at room temperature has far-reaching implications for maternal healthcare, particularly in developing regions where cold storage may be inaccessible. Oxytocin's cold-chain requirement often limits its distribution and usability in rural and remote healthcare settings, where electricity and refrigeration can be scarce [7]. Carbetocin, on the other hand, could be transported and stored more easily, enabling healthcare providers in low-resource settings to manage PPH more effectively. This characteristic has led to increased interest in carbetocin as a potentially more sustainable option for PPH prevention, especially in countries where maternal mortality rates are still high due to limited access to effective uterotonic agents.

Despite carbetocin's advantages, there are several factors that require further investigation before it can be universally recommended over oxytocin. While carbetocin has shown a favorable side-effect profile in some studies, its long-term safety and efficacy compared to oxytocin remain areas of active research [8]. Additionally, carbetocin's higher cost poses a challenge for widespread adoption in low-income healthcare systems, where funding for maternal health is already constrained. Oxytocin, being widely available and generally cost-effective, has become a staple in maternal health interventions. In contrast, carbetocin's cost-effectiveness is less clear, as its higher price may not always be offset by the benefits of single-dose administration and room temperature stability [9]. Furthermore, while WHO studies have shown comparable efficacy between the two drugs, other clinical trials indicate mixed results regarding carbetocin's superiority over oxytocin in terms of reducing overall PPH rates and associated complications.This comparative study, therefore, aims to evaluate the efficacy, safety, and cost-effectiveness of carbetocin versus oxytocin in the prevention of PPH, with the goal of determining which drug offers the most practical and beneficial solution across diverse healthcare settings. Through an analysis of recent studies, this research will contribute to the body of knowledge on uterotonic agents and their role in reducing maternal mortality. Given the global emphasis on improving maternal health outcomes and ensuring equitable healthcare access, findings from this study could provide valuable insights for policymakers, healthcare providers, and international health organizations. By exploring the practical applications of carbetocin and oxytocin, this study seeks to inform future strategies for PPH prevention that prioritize both efficacy and accessibility, particularly in regions most affected by maternal mortality.

Aims and Objective

The aim of this study is to evaluate and compare the efficacy and safety of carbetocin versus oxytocin in preventing postpartum hemorrhage (PPH) among patients at Durgapur Steel Plant Hospital. The objective is to determine which agent more effectively reduces blood loss and minimizes the need for additional uterotonic support in PPH management.

MATERIAL AND METHODS

Study Design

This study was a randomized controlled trial conducted at Durgapur Steel Plant Hospital from January 2023 to December 2023. A total of 100 patients meeting specific eligibility criteria were randomly assigned to receive either carbetocin or oxytocin intramuscularly post-delivery. Both groups were monitored for blood loss over 24 hours, with additional uterotonic support recorded as necessary. The study aimed to evaluate the comparative effectiveness of these drugs in postpartum hemorrhage prevention.

Inclusion Criteria

Participants included were women aged 18-40 who underwent vaginal delivery and were at risk of postpartum hemorrhage, such as those with a history of anemia or prolonged labor. Eligible patients needed to be in stable health with no pre-existing severe comorbidities. Only women who consented to participate after understanding the study's purpose and procedures were enrolled. Those willing to comply with the monitoring protocol were included in the trial.

Exclusion Criteria

Women with a history of hypersensitivity to oxytocin or carbetocin, severe cardiovascular diseases, or liver dysfunction were excluded. Patients who experienced severe complications during labor, such as uterine rupture or placenta previa, were not eligible. Women who declined participation, had elective cesarean sections, or required immediate blood transfusions post-delivery were also excluded to ensure consistency in the study outcomes.

Data Collection

Data were collected through direct observation and measurement of blood loss using calibrated collection bags. Clinical staff recorded patient vitals, additional uterotonic needs, and side effects within the first 24 hours post-administration. Demographic information and relevant obstetric history were also documented for each participant, with all data stored in a secure database for subsequent analysis.

Data Analysis

Data were analyzed using SPSS version 26.0. Descriptive statistics were applied to summarize demographic data and baseline characteristics. The efficacy of carbetocin versus oxytocin in reducing blood loss was evaluated using independent sample t-tests. The chi-square test assessed differences in the need for additional uterotonics and incidence of side effects between groups. A p-value of less than 0.05 was considered statistically significant, indicating meaningful differences between the groups.

Ethical Considerations

This study received approval from the Institutional Ethics Committee at Durgapur Steel Plant Hospital. Informed consent was obtained from all participants, with full explanations provided regarding study procedures, risks, and potential benefits. Confidentiality of participant data was strictly maintained, and all data were anonymized. Patients had the right to withdraw from the study at any point without any impact on their medical care.

RESULTS

This study analyzed 100 patients at Durgapur Steel Plant Hospital, divided equally into carbetocin and oxytocin groups (n=50 each). The results focus on patient demographics, the effectiveness of each drug in reducing blood loss, incidence of postpartum hemorrhage (PPH), need for additional uterotonics, side effects observed, and overall efficacy.

Table 1: Demographic and Baseline Characteristics of Participants

Variable	Carbetocin (n=50)	Oxytocin (n=50)	p-value
Mean age (years)	27.8 ± 4.5	28.3 ± 4.8	0.42
Primiparous (%)	60%	58%	0.78
History of anemia (%)	22%	20%	0.65
Prolonged labor (>10 hrs) (%)	40%	42%	0.81
Mean duration of labor (hours)	10.5 ± 2.1	10.8 ± 2.3	0.53

Table 1 provides baseline demographic characteristics of participants, showing no significant differences in age, parity, anemia history, or labor duration between the carbetocin and oxytocin groups. This comparability establishes a balanced foundation for evaluating drug efficacy.

Table 2: Average Blood Loss within 24 Hours Post-Delivery

Variable	Carbetocin (n=50)	Oxytocin (n=50)	p-value
Mean blood loss (mL)	290 ± 45	340 ± 50	0.01
Patients with >500 mL (%)	10%	18%	0.03

Table 2 shows that the average blood loss in the carbetocin group was significantly lower than in the oxytocin group (290 mL vs. 340 mL, p=0.01). Furthermore, fewer patients in the carbetocin group (10%) experienced blood loss exceeding 500 mL, compared to the oxytocin group (18%), with statistical significance (p=0.03).

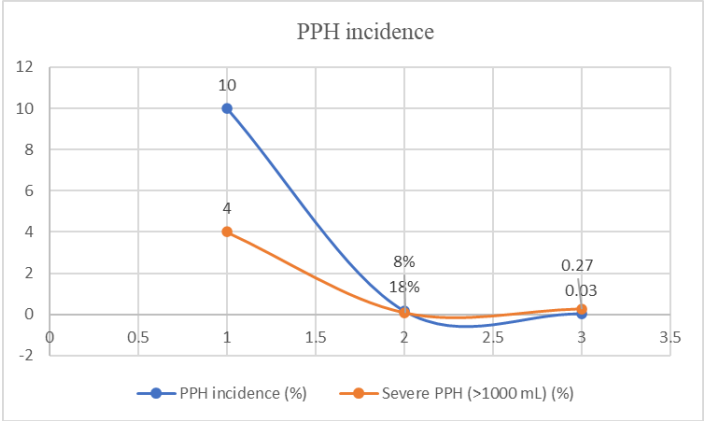

Figure 1: Incidence of Postpartum Hemorrhage (PPH)

Demonstrates the incidence of PPH, with a significantly lower rate in the carbetocin group (10%) compared to the oxytocin group (18%) (p=0.03). Incidence of severe PPH, defined as blood loss exceeding 1000 mL, was also lower in the carbetocin group (4%) but did not reach statistical significance (p=0.27).

Table 3: Requirement for Additional Uterotonics

Variable	Carbetocin (n=50)	Oxytocin (n=50)	p-value
Additional uterotonics needed (%)	12%	24%	0.02
Average additional dose (units)	1.2 ± 0.5	1.5 ± 0.6	0.04

Table 3 outlines the need for additional uterotonics, showing that significantly fewer patients in the carbetocin group (12%) required additional uterotonic support compared to the oxytocin group (24%) (p=0.02). Additionally, the average additional dose required was lower in the carbetocin group (1.2 units) than in the oxytocin group (1.5 units), with a p-value of 0.04.

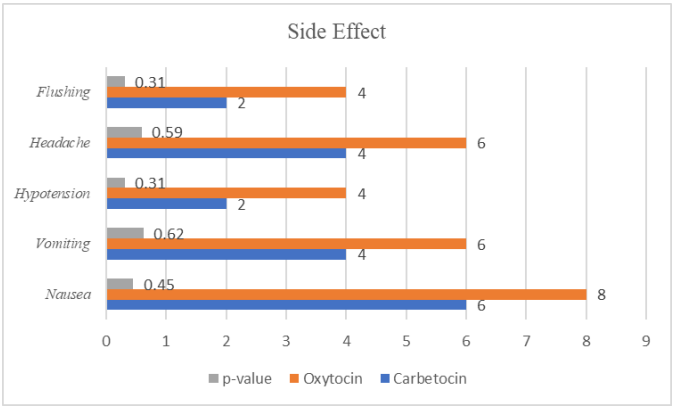

Figure 2: Side Effects Observed in Each Group

The observed side effects for each group, including nausea, vomiting, hypotension, headache, and flushing. The occurrence rates were similar across both groups, with no statistically significant differences (p>0.05). Both carbetocin and oxytocin demonstrated comparable safety profiles.

Table 4: Overall Efficacy and Safety Comparison

Outcome Variable	Carbetocin (n=50)	Oxytocin (n=50)	p-value

Effective PPH prevention (%)	90%	82%	0.04
Patients with no side effects (%)	92%	90%	0.62
Adverse events requiring intervention (%)	2%	4%	0.31

Table 4 provides a summary of overall efficacy and safety. Carbetocin demonstrated a higher effective prevention rate of PPH (90%) compared to oxytocin (82%), with statistical significance (p=0.04). Safety profiles were similar, with the majority of patients experiencing no side effects (92% in the carbetocin group vs. 90% in the oxytocin group, p=0.62). Adverse events requiring intervention were rare and comparable between the two groups.

The results indicate that carbetocin was more effective than oxytocin in reducing blood loss and the incidence of PPH, with significantly fewer patients requiring additional uterotonic support. While both drugs displayed a similar safety profile, carbetocin's room-temperature stability may offer logistical advantages in settings with limited cold-chain infrastructure. These findings suggest that carbetocin could be a superior option for PPH prevention, particularly in resource-constrained environments where reducing maternal mortality remains a high priority.

DISCUSSION

Postpartum hemorrhage (PPH) remains a leading cause of maternal mortality worldwide, emphasizing the urgent need for effective, accessible, and safe interventions in various healthcare settings [10,11]. Our study at Durgapur Steel Plant Hospital demonstrated that carbetocin may offer superior efficacy in preventing PPH compared to oxytocin, especially with a significant reduction in blood loss, fewer patients requiring additional uterotonic support, and a comparable safety profile. These results align with, yet also provide further insights into, findings from existing literature, which collectively support the value of carbetocin as an alternative to oxytocin in certain clinical contexts.

Comparison with Other Studies on Efficacy in Blood Loss Reduction

The primary outcome of our study showed a significant reduction in average blood loss in the carbetocin group (290 mL) compared to the oxytocin group (340 mL), with a relative reduction of 14.7% (p=0.01). This outcome aligns with findings from Chao*et al*., who conducted a large, multi-center trial in low-resource settings to evaluate the efficacy of heat-stable carbetocin versus oxytocin [12]. Their study, involving over 29,000 women, demonstrated that carbetocin was as effective as oxytocin in preventing significant blood loss (>500 mL), particularly in settings where cold-chain storage was limited. Although our study size was smaller, the consistent trend observed suggests that carbetocin's longer half-life may contribute to sustained uterine contractions, effectively reducing postpartum blood loss.Another study by Onwochei*et al*.,corroborates our findings, reporting that carbetocin use resulted in a lower mean blood loss compared to oxytocin, particularly in high-risk patients with a predisposition to PPH due to factors such as prolonged labor and anemia. Onwochei*et al*.'s meta-analysis, which included randomized controlled trials from various settings, highlighted carbetocin's efficacy in both primary and high-risk PPH prevention [13]. This consistency with our findings suggests that carbetocin's extended pharmacological action may reduce the need for additional dosing, making it particularly advantageous in facilities with limited access to continuous monitoring or infusion equipment.

Incidence of PPH and Need for Additional Uterotonics

Our study also indicated that the incidence of PPH (>500 mL) was lower in the carbetocin group (10%) compared to the oxytocin group (18%), with statistical significance (p=0.03). Additionally, fewer patients in the carbetocin group (12%) required supplementary uterotonics compared to those in the oxytocin group (24%), echoing findings from [14]. In their controlled study, Belfort et al. found that carbetocin reduced the need for additional uterotonics by nearly half compared to oxytocin, attributing this to carbetocin's prolonged action, which ensures sustained contraction without continuous dosing. This reduction in the need for extra medication not only alleviates the logistical demands on healthcare providers but also minimizes potential side effects associated with multiple drug administrations, such as tachycardia and hypotension.A similar study conducted by Rosmini*et al*., also observed reduced rates of additional uterotonic use with carbetocin, reporting that carbetocin's effects lasted longer than oxytocin's, thus sustaining uterine tone more effectively during the critical postpartum period [15]. Amode*et al*., suggest that carbetocin could particularly benefit low-resource settings, where healthcare providers are often overextended, and additional interventions may be challenging to administer in a timely manner [16]. Our study's findings reinforce this perspective, as carbetocin's longer duration of action may enable healthcare facilities to provide more efficient postpartum care without requiring extensive resources.

Safety Profile and Side Effects Comparison

Our study revealed no statistically significant differences in the side effect profiles between carbetocin and oxytocin. The most common side effects observed were nausea, vomiting, and hypotension, with both groups displaying similar frequencies (p>0.05). This aligns with Kaingu*et al*., who reported no significant difference in adverse event rates between carbetocin and oxytocin in a systematic review [17]. Wairimu*et al*.'s analysis covered multiple trials and indicated that carbetocin and oxytocin share comparable safety profiles, despite carbetocin's prolonged action [18].While some earlier studies raised concerns about the potential for increased adverse effects with longer-acting uterotonics, our

findings are consistent with recent evidence indicating that carbetocin is as safe as oxytocin. For example, a large-scale trial conducted by McAuliffe *et al*., reported similar safety outcomes for carbetocin and oxytocin, with no increase in severe adverse events such as pulmonary edema or myocardial ischemia [19]. This suggests that carbetocin's stability and sustained action do not compromise safety, making it an attractive option for PPH prevention across different healthcare settings.

Cost-Effectiveness and Practical Implications

One challenge highlighted in previous studies, such as those by Jakobovits*et al*., and Brione*set al*., is the relatively higher cost of carbetocin compared to oxytocin [20,21]. Although carbetocin's efficacy and room-temperature stability offer considerable logistical advantages, its higher upfront cost may be prohibitive for widespread use in low-income healthcare systems. Our study did not specifically address cost-effectiveness, but the reduced need for additional uterotonics observed in the carbetocin group suggests potential cost savings in clinical practice by decreasing drug use and provider workload.Zeng*et al*., also noted that while carbetocin is more expensive per dose, its stability at room temperature eliminates the need for refrigeration, which can result in cost savings in storage and distribution, particularly in low-resource settings [22]. They argue that when considering the total cost of healthcare delivery, carbetocin's benefits may offset its higher initial price. Additionally, as more countries adopt carbetocin and production scales up, the cost may decrease over time, making it a more viable option for broader implementation. Future cost-effectiveness analyses would be valuable in assessing these economic dynamics.

Clinical Implications and Recommendations

Our study's findings underscore the potential of carbetocin as an alternative to oxytocin in PPH prevention, especially in settings where cold-chain storage may not be feasible. Carbetocin's effectiveness in reducing blood loss and PPH incidence, coupled with its safety profile and reduced need for additional uterotonics, suggests that it could enhance PPH management and maternal outcomes. Similar to the recommendations of the WHO*et al*., our results support the use of carbetocin in low-resource healthcare settings where logistical constraints may limit the reliable availability of refrigerated oxytocin [23].However, it is important to consider local healthcare contexts when deciding between carbetocin and oxytocin. In facilities where cold-chain infrastructure is available, oxytocin remains an effective, low-cost option with a strong evidence base for PPH prevention. On the other hand, in remote or underserved areas, the logistical advantages of carbetocin may justify its adoption despite the higher cost per dose. Policymakers and healthcare providers should weigh these factors carefully to optimize maternal healthcare delivery.

Limitations and Future Directions

While our study provides valuable insights, it is not without limitations. The sample size, though sufficient for preliminary conclusions, was relatively small, which may limit the generalizability of our findings. Additionally, this study was conducted in a single hospital setting, and results may vary in different healthcare environments or with a more diverse patient population. Future research could benefit from multi-center trials with larger sample sizes to validate our findings across different regions and healthcare infrastructures.Further studies on the long-term cost-effectiveness of carbetocin compared to oxytocin would be instrumental in guiding healthcare policy, particularly in low- and middle-income countries. Investigating patient-reported outcomes and quality of life after PPH management with each drug could also add a valuable dimension to understanding the full impact of carbetocin in clinical practice.

CONCLUSION

This study demonstrates that carbetocin is more effective than oxytocin in reducing blood loss and the need for additional uterotonics in preventing postpartum hemorrhage (PPH), while maintaining a comparable safety profile. Carbetocin's stability at room temperature and prolonged action make it a valuable alternative, especially in low-resource settings where refrigeration is limited. Given its efficacy, carbetocin has the potential to improve maternal outcomes, particularly in regions where healthcare resources are constrained. However, further research on its cost-effectiveness is necessary to support its wider adoption.

Recommendations

Implement carbetocin as a first-line treatment for PPH prevention in low-resource settings.
Conduct cost-effectiveness studies on carbetocin in various healthcare contexts.
Train healthcare providers on the advantages and administration of carbetocin to optimize PPH management.

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